## SEQUENCE LISTING



- <110> Smith, Leonard A.
   Byrne, Michael P.
   Middlebrook, John L.
   Lapenotiere, Hugh
   Clayton, Michael A.
   Brown, Douglas R.
- <120> RECOMBINANT VACCINE AGAINST BOTULINUM NEUROTOXIN
- <130> A33626-A 067252.0107
- <140> 09/910,186
- <141> 2001-07-20
- <150> 09/611,419
- <151> 2000-07-06
- <150> PCT/US00/12890
- <151> 2000-05-12
- <150> 60/133,865
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- <150> 60/146,192
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tccaaaatca acatcggttc taaagttaac ttcgatccga tcgacaagaa tcaqatccaq 180
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cgtgttgtat tcaaatactc tcagatgatc aacatctctg actacatcaa tcgctggatc 480
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Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
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Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
                    70
Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
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Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
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Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
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Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
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Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
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Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
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Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
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Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn
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Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg
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Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn
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Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys
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Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg
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Val Tyr Ile Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr
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Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile
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Pro Asp Val Gly Asn Leu Ser Gln Val Val Wat Lys Ser Lys Asn
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Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn
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Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala
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Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser
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aacatcggtt ctaaagttaa cttcgatccg atcgacaaga atcagatcca gctgttcaat 180
ctggaatctt ccaaaatcga agttatcctg aagaatgcta tcgtatacaa ctctatgtac 240
gaaaacttct ccacctcctt ctggatccgt atcccgaaat acttcaactc catctctctg 300
aacaatgaat acaccatcat caactgcatg gaaaacaatt ctggttggaa agtatctctg 360
aactacggtg aaatcatctg gactctgcag gacactcagg aaatcaaaca gcgtgttgta 420
ttcaaatact ctcagatgat caacatctct gactacatca atcgctggat cttcgttacc 480
atcaccaaca atcgtctgaa taactccaaa atctacatca acggccgtct gatcgaccag 540
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ggttgtcgtg acactcaccg ctacatctgg atcaaatact tcaatctgtt cgacaaagaa 660
ctgaacgaaa aagaaatcaa agacctgtac gacaaccagt ccaattctgg tatcctgaaa 720
gacttetggg gtgactacet geagtaegae aaacegtaet acatgetgaa tetgtaegat 780
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185

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aaattcatca tcaagaaata cgcgtctggt aacaaggaca atatcgttcg caacaatgat 960
cgtgtataca tcaatgttgt agttaagaac aaagaatacc gtctggctac caatgcttct 1020
caggctggtg tagaaaagat cttgtctgct ctggaaatcc cggacgttgg taatctgtct 1080
caggtagttg taatgaaatc caagaacgac cagggtatca ctaacaaatg caaaatgaat 1140
ctgcaggaca acaatggtaa cgatatcggt ttcatcggtt tccaccagtt caacaatatc 1200
gctaaactgg ttgcttccaa ctggtacaat cgtcagatcg aacgttcctc tcgcactctq 1260
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                            40
Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile Glu Val
Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn Phe Ser
                    70
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Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile Ser Leu
                                    90
Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp
            100
                                105
Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln Asp Thr
                            120
                                                 125
Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met Ile Asn
                        135
Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn Asn
                    150
                                        155
Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu Ile Asp Gln
                                                         175
Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn Ile Met
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Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile Trp Ile Lys
                            200
Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu Ile Lys Asp
                        215
                                            220
Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp Phe Trp Gly
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                                        235
Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn Leu Tyr Asp
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Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly Tyr Met
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Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile Tyr Leu

280

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gtattcgaag aatacaaaga ctacttctgc atctccaaat ggtacctgaa ggaagttaaa 1260
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                                    10
Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala
            20
Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe
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40 Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp 75 Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys 105 Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn 120 125 Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile 135 Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu 150 Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp 170 Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys 180 185 Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe 200 Ser Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr 215 220 Lys Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro 230 235 Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn 245 250 Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr 265 Arg Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu 280 285 Tyr Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser 295 300 Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe 310 315 Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys Tyr Phe Lys 325 330 Lys Glu Glu Lys Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu 340 345 Leu Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr 360 Ser Cys Gln Leu Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile 380 Gly Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu 390 395 Glu Tyr Lys Asp Tyr Phe Cys Ile Ser Lys Trp Tyr Leu Lys Glu Val 410 Lys Arg Lys Pro Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile 420 425 Pro Lys Asp Glu Gly Trp Thr Glu

<210> 9

<211> 1371

<212> DNA

<213> Artificial Sequence

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aacatgaaga totacatcaa cggtaagctg atcgacacca tcaaggtcaa ggagttgacc 600
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Lys Asp Ile Ile Asn Glu Tyr Phe Asn Asn Ile Asn Asp Ser Lys Ile
Leu Ser Leu Gln Asn Arg Lys Asn Thr Leu Val Asp Thr Ser Gly Tyr
                            40
Asn Ala Glu Val Ser Glu Glu Gly Asp Val Gln Leu Asn Pro Ile Phe
Pro Phe Asp Phe Lys Leu Gly Ser Ser Gly Glu Asp Arg Gly Lys Val
                                        75
Ile Val Thr Gln Asn Glu Asn Ile Val Tyr Asn Ser Met Tyr Glu Ser
                                    90
Phe Ser Ile Ser Phe Trp Ile Arg Ile Asn Lys Trp Val Ser Asn Leu
            100
                                105
Pro Gly Tyr Thr Ile Ile Asp Ser Val Lys Asn Asn Ser Gly Trp Ser
                            120
Ile Gly Ile Ile Ser Asn Phe Leu Val Phe Thr Leu Lys Gln Asn Glu
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Pro Gly Tyr Asn Lys Trp Phe Phe Val Thr Val Thr Asn Asn Met Met
                165
                                     170
Gly Asn Met Lys Ile Tyr Ile Asn Gly Lys Leu Ile Asp Thr Ile Lys
                                 185
Val Lys Glu Leu Thr Gly Ile Asn Phe Ser Lys Thr Ile Thr Phe Glu
                             200
                                                 205
Ile Asn Lys Ile Pro Asp Thr Gly Leu Ile Thr Ser Asp Ser Asp Asn
                        215
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Ile Asn Met Trp Ile Arg Asp Phe Tyr Ile Phe Ala Lys Glu Leu Asp
                    230
                                         235
Gly Lys Asp Ile Asn Ile Leu Phe Asn Ser Leu Gln Tyr Thr Asn Val
                                     250
Val Lys Asp Tyr Trp Gly Asn Asp Leu Arg Tyr Asn Lys Glu Tyr Tyr
                                 265
Met Val Asn Ile Asp Tyr Leu Asn Arg Tyr Met Tyr Ala Asn Ser Arg
                             280
                                                 285
Gln Ile Val Phe Asn Thr Arg Arg Asn Asn Asn Asp Phe Asn Glu Gly
                        295
                                             300
Tyr Lys Ile Ile Lys Arg Ile Arg Gly Asn Thr Asn Asp Thr Arg
                    310
                                         315
Val Arg Gly Gly Asp Ile Leu Tyr Phe Asp Met Thr Ile Asn Asn Lys
                325
                                     330
Ala Tyr Asn Leu Phe Met Lys Asn Glu Thr Met Tyr Ala Asp Asn His
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Ser Thr Glu Asp Ile Tyr Ala Ile Gly Leu Arg Glu Gln Thr Lys Asp
                            360
Ile Asn Asp Asn Ile Ile Phe Gln Ile Gln Pro Met Asn Asn Thr Tyr
                        375 .
                                             380
Tyr Tyr Ala Ser Gln Ile Phe Lys Ser Asn Phe Asn Gly Glu Asn Ile
                    390 -
                                        395
Ser Gly Ile Cys Ser Ile Gly Thr Tyr Arg Phe Arg Leu Gly Gly Asp
                                     410
Trp Tyr Arg His Asn Tyr Leu Val Pro Thr Val Lys Gln Gly Asn Tyr
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Ala Ser Leu Leu Glu Ser Thr Ser Thr His Trp Gly Phe Val Pro Val
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Ser Glu
    450
<210> 11
<211> 1374
<212> DNA
<213> Artificial Sequence
<223> Synthetic construct based on BoNTD Hc
<400> 11
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aacatettet eetacaecaa caacteettg ttgaaggaca teateaaega gtaetteaae 120
tccatcaacg actccaagat cttgtccttg cagaacaaga agaacgcctt ggtcgacacc 180
teeggttaca acgeegaggt cagagteggt gacaacgtee agttgaacac catetacace 240
aacgacttca agttgtcctc ttccggtgac aagatcatcg tcaacttgaa caacaacatc 300
ttgtactccg ccatctacga gaactcctct gtctccttct ggatcaagat ctccaaggac 360
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ttgaccaact cccacaacga gtacaccatc atcaactcca tcgagcagaa ctccggttgg 420
aagttgtgta teegtaaegg taacategag tggatettge aggaegteaa eegtaagtae 480
aagteettga tettegaeta eteegagtee ttgteecaca eeggttacae caacaagtgg 540
ttcttcgtca ccatcaccaa caacatcatg ggttacatga agttgtacat caacggtgag 600
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ttcggtatcg acgagaacat cgacgagaac cagatgttgt ggatccgtga cttcaacatc 720
ttetecaagg agetgtecaa egaggacate aacategtet aegagggtea gateetgagg 780
aacgtcatca aggactactg gggtaaccca ctgaagttcg acaccgagta ctacatcatc 840
aacgacaact acatcgaccg ttacatcgcc ccagagtcca acgtcctggt cctggtccag 900
taccctgacc gttccaagct gtacaccggt aaccctatca ccatcaagtc cgtctccgac 960
aagaaccett acteeegtat eetgaaeggt gacaacatea teetgeacat getgtacaac 1020
tecegtaagt acatgateat eegtgaeace gacaceatet aegecaeeca gggtggtgae 1080
tgttcccaga actgtgtcta cgccctgaag ctgcagtcca acctgggtaa ctacggtatc 1140
ggtatettet ceateaagaa categtetee aagaacaagt aetgeteeca gatettetee 1200
teetteegtg agaacaccat getgetggee gacatetaca ageettggeg ttteteette 1260
aagaacgcct acactcctgt cgccgtcacc aactacgaga ccaagctgct gtccacctcc 1320
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<210> 12
<211> 451
<212> PRT
<213> Artificial Sequence
<220>
<223> Encoded polypeptide of a synthetic construct based
      on BoNTD Hc
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Phe Asn Ile Phe Ser Tyr Thr Asn Asn Ser Leu Leu Lys Asp Ile Ile
Asn Glu Tyr Phe Asn Ser Ile Asn Asp Ser Lys Ile Leu Ser Leu Gln
                            40
Asn Lys Lys Asn Ala Leu Val Asp Thr Ser Gly Tyr Asn Ala Glu Val
                        55
                                            60
Arg Val Gly Asp Asn Val Gln Leu Asn Thr Ile Tyr Thr Asn Asp Phe
                    70
                                        75
Lys Leu Ser Ser Ser Gly Asp Lys Ile Ile Val Asn Leu Asn Asn
                                    90
Ile Leu Tyr Ser Ala Ile Tyr Glu Asn Ser Ser Val Ser Phe Trp Ile
                                105
Lys Ile Ser Lys Asp Leu Thr Asn Ser His Asn Glu Tyr Thr Ile Ile
                            120
                                                125
Asn Ser Ile Glu Gln Asn Ser Gly Trp Lys Leu Cys Ile Arg Asn Gly
                        135
                                            140
Asn Ile Glu Trp Ile Leu Gln Asp Val Asn Arg Lys Tyr Lys Ser Leu
                    150
                                        155
Ile Phe Asp Tyr Ser Glu Ser Leu Ser His Thr Gly Tyr Thr Asn Lys
                                    170
                                                        175
Trp Phe Phe Val Thr Ile Thr Asn Asn Ile Met Gly Tyr Met Lys Leu
            180
                                185
Tyr Ile Asn Gly Glu Leu Lys Gln Ser Gln Lys Ile Glu Asp Leu Asp
                            200
                                                205
Glu Val Lys Leu Asp Lys Thr Ile Val Phe Gly Ile Asp Glu Asn Ile
                        215
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Asp Glu Asn Gln Met Leu Trp Ile Arg Asp Phe Asn Ile Phe Ser Lys

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225
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Glu Leu Ser Asn Glu Asp Ile Asn Ile Val Tyr Glu Gly Gln Ile Leu
                                     250
Arg Asn Val Ile Lys Asp Tyr Trp Gly Asn Pro Leu Lys Phe Asp Thr
                                 265
Glu Tyr Tyr Ile Ile Asn Asp Asn Tyr Ile Asp Arg Tyr Ile Ala Pro
                             280
                                                 285
Glu Ser Asn Val Leu Val Leu Val Gln Tyr Pro Asp Arg Ser Lys Leu
                         295
                                             300
Tyr Thr Gly Asn Pro Ile Thr Ile Lys Ser Val Ser Asp Lys Asn Pro
                    310
                                         315
Tyr Ser Arg Ile Leu Asn Gly Asp Asn Ile Ile Leu His Met Leu Tyr
                                     330
Asn Ser Arg Lys Tyr Met Ile Ile Arg Asp Thr Asp Thr Ile Tyr Ala
            340
Thr Gln Gly Gly Asp Cys Ser Gln Asn Cys Val Tyr Ala Leu Lys Leu
                             360
Gln Ser Asn Leu Gly Asn Tyr Gly Ile Gly Ile Phe Ser Ile Lys Asn
Ile Val Ser Lys Asn Lys Tyr Cys Ser Gln Ile Phe Ser Ser Phe Arg
                    390
                                         395
Glu Asn Thr Met Leu Leu Ala Asp Ile Tyr Lys Pro Trp Arg Phe Ser
                405
                                     410
Phe Lys Asn Ala Tyr Thr Pro Val Ala Val Thr Asn Tyr Glu Thr Lys
            420
                                 425
Leu Leu Ser Thr Ser Ser Phe Trp Lys Phe Ile Ser Arg Asp Pro Gly
                            440
                                                 445
Trp Val Glu
    450
<210> 13
<211> 1400
<212> DNA
<213> Artificial Sequence
<223> Synthetic construct based on BoNTE Hc
<400> 13
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aacaagttct tcaagagaat taagtcttct tccgttttaa acatgagata caagaatgat 180
aaatacgtcg acacttccgg ttacgactcc aatatcaaca ttaacggtga cgtgtacaag 240
tacccaacta acaaaaacca attoggtato tacaacgaca agottactga gotgaacato 300
tctcaaaacg actacattat ctacgacaac aagtacaaga acttctctat ttctttctgg 360
gtcaggattc ctaactacga caacaagatc gtcaacgtta acaacgagta cactatcatc 420
aactgtatga gagacaacaa ctccggttgg aaggtctctc ttaaccacaa cgagatcatt 480
tggaccttgc aagacaacgc aggtattaac caaaagttag cattcaacta cggtaacgca 540
aacggtattt ctgactacat caacaagtgg attttcgtca ctatcactaa cgacagatta 600
ggtgactcta agctttacat taacggtaac ttaatcgacc aaaagtccat tttaaactta 660
ggtaacattc acgtttctga caacatctta ttcaagatcg ttaactgcag ttacaccaga 720
tacattggca ttagatactt caacattttc gacaaggagt tagacgagac cgagattcaa 780
actttataca gcaacgaacc taacaccaat attttgaagg acttctgggg taactacttg 840
ctttacgaca aggaatacta cttattaaac gtgttaaagc caaacaactt cattgatagg 900
agaaaggatt ctactttaag cattaacaac atcagaagca ctattctttt agctaacaga 960
ttatactctg gtatcaaggt taagatccaa agagttaaca actcttctac taacgataac 1020
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cttgttagaa agaacgatca ggtctatatt aacttcgtcg ctagcaagac tcacttattc 1080 ccattatatg ctgataccgc taccaccaac aaggagaaga ccatcaagat ctcctcctct 1140 ggcaacagat ttaaccaagt cgtcgttatg aactccgtcg gtaacaactg taccatgaac 1200 tttaaaaata ataatggaaa taatattggg ttgttaggtt tcaaggcaga tactgtagtt 1260 gctagtactt ggtattatac ccacatgaga gatcacacca acagcaatgg atgtttttgg 1320 aactttattt ctgaagaaca tggatggcaa gaaaaataat agggatccgc ggccqcacgc 1380 gtcccgggac tagtgaattc <210> 14 <211> 449 <212> PRT <213> Artificial Sequence <223> Encoded polypeptide of a synthetic construct based on BoNTE Hc <400> 14 Met Gly Glu Ser Gln Gln Glu Leu Asn Ser Met Val Thr Asp Thr Leu 10 Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr Thr Asp Asp Lys Ile 20 25 Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys Ser Ser Ser 40 Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp Thr Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys Tyr Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Thr Glu Leu Asn 90 Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr Lys Asn Phe 100 105 Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn Lys Ile Val 120 Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg Asp Asn Asn 135 140 Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile Trp Thr Leu 150 155 Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn Tyr Gly Asn 170 175 Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe Val Thr Ile 185 Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr Ile Asn Gly Asn Leu 200 205 Ile Asp Gln Lys Ser Ile Leu Asn Leu Gly Asn Ile His Val Ser Asp 215 Asn Ile Leu Phe Lys Ile Val Asn Cys Ser Tyr Thr Arg Tyr Ile Gly 230 235 Ile Arg Tyr Phe Asn Ile Phe Asp Lys Glu Leu Asp Glu Thr Glu Ile 250 Gln Thr Leu Tyr Ser Asn Glu Pro Asn Thr Asn Ile Leu Lys Asp Phe 260 265 Trp Gly Asn Tyr Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu Asn Val 280 Leu Lys Pro Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr Leu Ser 295

Ile Asn Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu Tyr Ser

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305
                    310
                                         315
Gly Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr Asn Asp
Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val Ala Ser
            340
                                 345
Lys Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr Asn Lys
                            360
Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe Asn Gln Val
                        375
                                            380
Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met Asn Phe Lys Asn
                    390
                                        395
Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe Lys Ala Asp Thr Val
                405
                                    410
Val Ala Ser Thr Trp Tyr Tyr Thr His Met Arg Asp His Thr Asn Ser
Asn Gly Cys Phe Trp Asn Phe Ile Ser Glu Glu His Gly Trp Gln Glu
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Lys
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<211> 1317
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTF Hc
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atctccggtt acggttccaa catctccatc aacggtgacg tctacatcta ctccaccaat 180
agaaaccagt tcggaatcta ctcctccaag ccttccgagg tcaacatcgc tcagaacaac 240
gacatcatct acaacggaag ataccagaac ttctccatct ccttctgggt ccgtatccca 300
aagtacttca acaaggtcaa cctgaataac gagtacacca tcatcgactg catccgtaac 360
aataactccg gatggaagat ctccctgaac tacaacaaga tcatctggac cctgcaggac 420
accgccggta acaatcagaa gttggtcttc aactacaccc agatgatctc catctccgac 480
tacatcaaca agtggatctt cgtcaccatc accaataacc gtttgggaaa ctccagaatc 540
tacatcaacg gtaacttgat cgacgagaag tccatctcca acttgggtga catccacgtc 600
teegacaaca ttttgtteaa gategteggt tgtaacgaca eeegttaegt egggateegt 660
tacttcaaag tcttcgacac tgagttgggt aagaccgaga tcgagacctt gtactccgac 720
gageetgace catecateet gaaggactte tggggtaact acetgetgta caacaaacgt 780
tactacttgc tgaacttgtt gcgtaccgac aagtccatca cccagaactc caacttcttg 840
aacatcaacc agcagagagg tgtctaccag aagccaaaca tcttctccaa caccagattg 900
tacaccggag tcgaggtcat tatcagaaag aacggatcta ctgatatttc caacaccgat 960
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tctaactcta acaactctct gggacaaatc atcgtcatgg actccatcgg taataactgt 1140
accatgaact tccagaacaa caacggtgga aacatcggtt tgttgggttt ccactccaac 1200
aacttggteg etteeteetg gtaetacaae aacateegta agaacacete etecaacggt 1260
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<210> 16
<211> 432
<212> PRT
<213> Artificial Sequence
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<223> Encoded polypeptide of a synthetic construct based on BoNTF  ${\mbox{Hc}}$ 

<400> 16 Met Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu 10 Tyr Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn 25 Asn Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn 40 Gly Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr 55 Ser Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile 70 Tyr Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile 90 Pro Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile 105 Asp Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr 120 Asn Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys 135 140 Leu Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn 150 155 Lys Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg 170 Ile Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu 185 Gly Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys 200 Asn Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr 215 Glu Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp 230 235 Pro Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys 245 250 Arg Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln 260 265 Asn Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys 280 Pro Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile 295 300 Ile Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val 310 315 Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu 325 330 Tyr Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile 345 Lys Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile 360 Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn 375 380 Asn Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val 390 Ala Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn

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405
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Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn
            420
                                425
<210> 17
<211> 1368
<212> DNA
<213> Artificial Sequence
<223> Synthetic construct based on BoNTG Hc
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tacggagcca ccatgaacgt cggttccgac gtcatcttca acgacatcgg taacggtcag 180
ttcaagctga acaactccga gaactccaac atcaccgccc accagtccaa gttcqtcqtc 240
tacgactcca tgttcgacaa cttctccatc aacttctggg tccgtacccc aaagtacaac 300
aacaacgaca tccagaccta cctgcagaac gagtacacca tcatctcctg tatcaagaac 360
gactccggtt ggaaggtctc catcaaggga aaccgtatca tctggaccct gatcgacgtc 420
aacgccaagt ccaagtccat cttcttcgag tactccatca aggacaacat ctccgactac 480
atcaacaagt ggttctccat caccatcacc aacgaccgtc tgggtaacgc caacatctac 540
atcaacggtt ccctgaagaa gtccgagaag atcctgaacc tggaccgtat caactcctcc 600
aacgacatcg acttcaagct gatcaactgt accgacacca ccaagttcgt ctggatcaag 660
gacticaaca tetteggieg tgagetgaac gecacegagg tetecteect qtactqqate 720
cagtcctcca ccaacaccct gaaggacttc tggggaaacc cactgcgtta cgacacccag 780
tactacctgt tcaaccaggg tatgcagaac atctacatca agtacttctc caaggcctcc 840
atgggtgaga ccgccctcg taccaacttc aacaacgccg ccatcaacta ccagaacctg 900
tacctgggtc tgcgtttcat catcaagaag gcctccaact cccgtaacat caacaacgac 960
aacatcgtcc gtgagggtga ctacatctac ctgaacatcg acaacatctc cgacgagtcc 1020
taccgtgtct acgtcctggt caactccaag gagatccaga cccagctgtt cctggcccca 1080
atcaacgacg accetacett ctacgacgte etgeagatea agaagtacta egagaagace 1140
acctacaact gtcagatcct gtgcgagaag gacaccaaga ccttcggact gttcggtatc 1200
ggtaagttcg tcaaggacta cggttacgtc tgggacacct acqacaacta cttctgtatc 1260
teccagtggt acetgegteg tateteegag aacateaaca agetgegtet gggatgtaac 1320
tggcagttca tcccagtcga cgagggttgg accgagtaat aggaattc
<210> 18
<211> 449
<212> PRT
<213> Artificial Sequence
<223> Encoded polypeptide of a synthetic construct based
      on BoNTG Hc
<400> 18
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                                    10
Ile Ser Ser Asn Ala Ile Leu Ser Leu Ser Tyr Arg Gly Gly Arg Leu
            20
                                25
                                                    30
Ile Asp Ser Ser Gly Tyr Gly Ala Thr Met Asn Val Gly Ser Asp Val
                            40
Ile Phe Asn Asp Ile Gly Asn Gly Gln Phe Lys Leu Asn Asn Ser Glu
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Asn Ser Asn Ile Thr Ala His Gln Ser Lys Phe Val Val Tyr Asp Ser

70 75 Met Phe Asp Asn Phe Ser Ile Asn Phe Trp Val Arq Thr Pro Lys Tyr 90 Asn Asn Asp Ile Gln Thr Tyr Leu Gln Asn Glu Tyr Thr Ile Ile 100 105 Ser Cys Ile Lys Asn Asp Ser Gly Trp Lys Val Ser Ile Lys Gly Asn 120 Arg Ile Ile Trp Thr Leu Ile Asp Val Asn Ala Lys Ser Lys Ser Ile 135 140 Phe Phe Glu Tyr Ser Ile Lys Asp Asn Ile Ser Asp Tyr Ile Asn Lys 150 155 Trp Phe Ser Ile Thr Ile Thr Asn Asp Arg Leu Gly Asn Ala Asn Ile 170 Tyr Ile Asn Gly Ser Leu Lys Lys Ser Glu Lys Ile Leu Asn Leu Asp 180 Arg Ile Asn Ser Ser Asn Asp Ile Asp Phe Lys Leu Ile Asn Cys Thr 200 Asp Thr Thr Lys Phe Val Trp Ile Lys Asp Phe Asn Ile Phe Gly Arg 215 Glu Leu Asn Ala Thr Glu Val Ser Ser Leu Tyr Trp Ile Gln Ser Ser 230 235 Thr Asn Thr Leu Lys Asp Phe Trp Gly Asn Pro Leu Arg Tyr Asp Thr 250 Gln Tyr Tyr Leu Phe Asn Gln Gly Met Gln Asn Ile Tyr Ile Lys Tyr 260 265 Phe Ser Lys Ala Ser Met Gly Glu Thr Ala Pro Arg Thr Asn Phe Asn 280 Asn Ala Ala Ile Asn Tyr Gln Asn Leu Tyr Leu Gly Leu Arg Phe Ile 295 300 Ile Lys Lys Ala Ser Asn Ser Arg Asn Ile Asn Asn Asp Asn Ile Val 310 315 Arg Glu Gly Asp Tyr Ile Tyr Leu Asn Ile Asp Asn Ile Ser Asp Glu 325 330 Ser Tyr Arg Val Tyr Val Leu Val Asn Ser Lys Glu Ile Gln Thr Gln 340 345 Leu Phe Leu Ala Pro Ile Asn Asp Asp Pro Thr Phe Tyr Asp Val Leu 360 365 Gln Ile Lys Lys Tyr Tyr Glu Lys Thr Thr Tyr Asn Cys Gln Ile Leu 375 Cys Glu Lys Asp Thr Lys Thr Phe Gly Leu Phe Gly Ile Gly Lys Phe 390 Val Lys Asp Tyr Gly Tyr Val Trp Asp Thr Tyr Asp Asn Tyr Phe Cys 410 Ile Ser Gln Trp Tyr Leu Arg Arg Ile Ser Glu Asn Ile Asn Lys Leu 420 425 Arg Leu Gly Cys Asn Trp Gln Phe Ile Pro Val Asp Glu Gly Trp Thr 440 Glu

<210> 19

<211> 1242

<212> DNA

<213> Artificial Sequence

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gaagetgetg aagaaaacat etetetggae etgatecage agtactacet gaettteaac 180
ttcgacaacg aaccggaaaa catctccatc gaaaacctqt cttccqacat catcqqtcaq 240
ctggaactga tgccgaacat cgaacgcttc ccgaacggca agaaatacga actggacaaa 300
tacaccatgt tecaetacet gegtgeteag gaattegaae aeggtaaate tegtateget 360
ctgactaact ccgttaacga agctctgctg aacccgtctc gcgtttacac cttcttctct 420
gaacagctgg tttacgactt caccgacgaa acttctgaag tttccaccac tgacaaaatc 540
getgacatea etateateat ecegtacate ggeceggete tgaacategg taacatgetg 600
tacaaagacg acttegttgg tgetetgate ttetetggeg etgttateet getggaatte 660
atcccggaaa tcgctatccc ggttctgggt accttcgctc tggtttccta catcgctaac 720
aaagttetga etgticagae categacaae getetgteta aaegtaaega aaaatgggae 780
gaagtttaca aatacatcgt tactaactgg ctggctaaag ttaacactca gatcgacctg 840
atccgtaaga agatgaaaga agctctggaa aaccaggctg aagctactaa agctatcatc 900
aactaccagt acaaccagta caccqaaqaa qaaaaqaaca acatcaactt caacatcqat 960
gacctgtcct ctaaactgaa cgaatccatc aacaaagcta tgatcaacat caacaaattc 1020
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ctggaagact tcgacgcttc cctgaaagac gctctgctga aatacatccq tqacaactac 1140
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gacatcccgt tccagctgtc caaatacgtt gacaaccagt aa
<210> 20
<211> 413
<212> PRT
<213> Artificial Sequence
<223> Encoded polypeptide of a synthetic construct based
      on BoNTA Hn
<400> 20
Met Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe
                                   10
Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu
                               25
Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser
Leu Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu
Pro Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln
                   70
                                       75
Leu Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr
Glu Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe
                               105
Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala
                           120
                                               125
Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val
                       135
Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val
                   150
                                       155
Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr
               165
                                   170
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Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn

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325
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Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val
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Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn
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                                                 365
Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu
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                                            380
Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu
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aagaacacct ccgagcatgg acaactagac ctgctctacc ctagtatcga cagtgagagt 240
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<212> PRT
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Asn Thr Asp Leu Pro Phe Ile Gly Asp Ile Ser Asp Val Lys Thr Asp
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<sup>&</sup>lt;211> 1161

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Artificial Sequence

<sup>&</sup>lt;220>

<sup>&</sup>lt;223> Synthetic construct based on BoNTD Hn

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accaacgttc aaaactactc cgacaagttc tctttggacg agtccatcct ggacggtcag 180
gtcccaatca acccagagat cgtcgaccca ctqttgccaa acqtcaacat ggagccattg 240
aacttgccag gtgaggagat cgtcttctac gacgacatca ccaaqtacqt cqactacttq 300
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accaecteeg tegaggagge ettgggttae tetaacaaga tetacaectt cetgecatee 420
ttggctgaga aggttaacaa gggtgttcaa gctggtttgt tcctgaactg qqccaacqag 480
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gtctccgtca tcatcccata catcggtcca gccttgaaca tcggtaactc cgccctgaga 600
ggtaacttca accaggeett egecacegee ggtgtegeet teetgetgga gggttteeca 660
gagttcacca tcccagccct gggtgtcttc accttctact cctccatcca ggagagagag 720
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Glu Asn Lys Ile Ile Thr Asp Glu Thr Asn Val Gln Asn Tyr Ser Asp
                            40
Lys Phe Ser Leu Asp Glu Ser Ile Leu Asp Gly Gln Val Pro Ile Asn
                        55
Pro Glu Ile Val Asp Pro Leu Leu Pro Asn Val Asn Met Glu Pro Leu
                    70
                                        75
Asn Leu Pro Gly Glu Glu Ile Val Phe Tyr Asp Asp Ile Thr Lys Tyr
                                    90
Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser
            100
                                105
Asn Asn Val Glu Asn Ile Thr Leu Thr Thr Ser Val Glu Glu Ala Leu
                            120
                                                125
Gly Tyr Ser Asn Lys Ile Tyr Thr Phe Leu Pro Ser Leu Ala Glu Lys
                        135
                                            140
Val Asn Lys Gly Val Gln Ala Gly Leu Phe Leu Asn Trp Ala Asn Glu
                    150
                                        155
Val Val Glu Asp Phe Thr Thr Asn Ile Met Lys Lys Asp Thr Leu Asp
                                    170
Lys Ile Ser Asp Val Ser Val Ile Ile Pro Tyr Ile Gly Pro Ala Leu
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Asn Ile Gly Asn Ser Ala Leu Arg Gly Asn Phe Asn Gln Ala Phe Ala

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Thr Ala Gly Val Ala Phe Leu Leu Glu Gly Phe Pro Glu Phe Thr Ile
Pro Ala Leu Gly Val Phe Thr Phe Tyr Ser Ser Ile Gln Glu Arg Glu
                    230
                                        235
Lys Ile Ile Lys Thr Ile Glu Asn Cys Leu Glu Gln Arg Val Lys Arg
                                    250
Trp Lys Asp Ser Tyr Gln Trp Met Val Ser Asn Trp Leu Ser Arg Ile
            260
                                265
Thr Thr Gln Phe Asn His Ile Asn Tyr Gln Met Tyr Asp Ser Leu Ser
        275
                            280
                                                285
Tyr Gln Ala Asp Ala Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys
                        295
Tyr Ser Gly Ser Asp Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu
                    310
                                        315
Lys Asn Ser Leu Asp Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn
                                    330
Lys Phe Ile Arg Glu Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu
                                345
Pro Lys Val Ile Asp Glu Leu Asn Lys Phe Asp Leu Arg Thr Lys Thr
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Glu Leu Ile Asn Leu Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu
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Val Asp
385
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<211> 1149
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aactacgaaa acgacctgga ccaggtcatc ctaaacttca actccgagtc cqcccctgqt 180
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ttagacgctc agaaggtgcc cgagggtgag aacaacgtca atctcacctc ttcaattgac 360
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200

205

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355 360 365
Thr Tyr Leu Leu Asn Tyr Ile Ile Gln His Gly Ser Ile Leu

<210> 28

370 375 380

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 ctaaacaaca actaccggaa caacttggat gaggttattt tggattacaa ctcacagacc 180
 atccctcaaa tttccaaccg taccttaaac actcttgtcc aagacaactc ctacgttcca 240
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 Lys Glu Ile Asp Asp Thr Thr Asn Leu Asn Asn Asn Tyr Arg Asn Asn
                             40
                                                 45
 Leu Asp Glu Val Ile Leu Asp Tyr Asn Ser Gln Thr Ile Pro Gln Ile
                         55
                                             60
Ser Asn Arg Thr Leu Asn Thr Leu Val Gln Asp Asn Ser Tyr Val Pro
                     70
                                         75
Arg Tyr Asp Ser Asn Gly Thr Ser Glu Ile Glu Glu Tyr Asp Val Val
                                     90
Asp Phe Asn Val Phe Phe Tyr Leu His Ala Gln Lys Val Pro Glu Gly
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105 Glu Thr Asn Ile Ser Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu Glu

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ataaaagaaa gaatgtacaa tgctttaaat aatcaatcac aagcaataga aaaaataata 900
gaagatcaat ataatagata tagtgaagaa gataaaatga atattaacat tgattttaat 960
gatatagatt ttaaacttaa tcaaagtata aatttagcaa taaacaatat agatgatttt 1020
ataaaccaat gttctatatc atatctaatg aatagaatga ttccattagc tgtaaaaaag 1080
ttaaaagact ttgatgataa tcttaagaga gatttattgg agtatataga tacaaatgaa 1140
ctatatttac ttgatgaagt aaatattcta aaatcaaaag taaatagaca cctaaaagac 1200
agtataccat ttgatctttc actatatacc taa
                                                                   1233
<210> 32
<211> 410
<212> PRT
<213> Artificial Sequence
<220>
<223> Encoded polypeptide of a synthetic construct based
      on BoNTG Hn
<400> 32
Met Ala Lys Asn Thr Gly Lys Ser Glu Gln Cys Ile Ile Val Asn Asn
                                    10
Glu Asp Leu Phe Phe Ile Ala Asn Lys Asp Ser Phe Ser Lys Asp Leu
Ala Lys Ala Glu Thr Ile Ala Tyr Asn Thr Gln Asn Asn Thr Ile Glu
                            40
Asn Asn Phe Ser Ile Asp Gln Leu Ile Leu Asp Asn Asp Leu Ser Ser
Gly Ile Asp Leu Pro Asn Glu Asn Thr Glu Pro Phe Thr Asn Phe Asp
                                        75
Asp Ile Asp Ile Pro Val Tyr Ile Lys Gln Ser Ala Leu Lys Lys Ile
                                    90
Phe Val Asp Gly Asp Ser Leu Phe Glu Tyr Leu His Ala Gln Thr Phe
            100
                                105
Pro Ser Asn Ile Glu Asn Leu Gln Leu Thr Asn Ser Leu Asn Asp Ala
                            120
Leu Arg Asn Asn Asn Lys Val Tyr Thr Phe Phe Ser Thr Asn Leu Val
Glu Lys Ala Asn Thr Val Val Gly Ala Ser Leu Phe Val Asn Trp Val
                    150
                                        155
Lys Gly Val Ile Asp Asp Phe Thr Ser Glu Ser Thr Gln Lys Ser Thr
                                    170
Ile Asp Lys Val Ser Asp Val Ser Ile Ile Ile Pro Tyr Ile Gly Pro
                                185
Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Glu Asn Phe Lys Asn Ala
                            200
                                                205
Phe Glu Ile Gly Gly Ala Ala Ile Leu Met Glu Phe Ile Pro Glu Leu
                        215
Ile Val Pro Ile Val Gly Phe Phe Thr Leu Glu Ser Tyr Val Gly Asn
                    230
                                        235
Lys Gly His Ile Ile Met Thr Ile Ser Asn Ala Leu Lys Lys Arg Asp
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250

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Gln Lys Trp Thr Asp Met Tyr Gly Leu Ile Val Ser Gln Trp Leu Ser
            260
                                265
Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Arg Met Tyr Asn Ala
                            280
Leu Asn Asn Gln Ser Gln Ala Ile Glu Lys Ile Ile Glu Asp Gln Tyr
                        295
                                            300
Asn Arg Tyr Ser Glu Glu Asp Lys Met Asn Ile Asn Ile Asp Phe Asn
                    310
                                        315
Asp Ile Asp Phe Lys Leu Asn Gln Ser Ile Asn Leu Ala Ile Asn Asn
                                    330
Ile Asp Asp Phe Ile Asn Gln Cys Ser Ile Ser Tyr Leu Met Asn Arg
                                345
Met Ile Pro Leu Ala Val Lys Lys Leu Lys Asp Phe Asp Asp Asn Leu
                            360
                                                365
Lys Arg Asp Leu Leu Glu Tyr Ile Asp Thr Asn Glu Leu Tyr Leu Leu
                        375
                                            380
Asp Glu Val Asn Ile Leu Lys Ser Lys Val Asn Arg His Leu Lys Asp
                    390
                                        395
Ser Ile Pro Phe Asp Leu Ser Leu Tyr Thr
                405
<210> 33
<211> 1314
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTF Hc
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aaaaaaatca aagacaactc tatcctggac atgcgttacg aaaacaacaa attcatcgac 120
atctctggct atggttctaa catctctatc aacggtgacg tctacatcta ctctactaac 180
cgcaaccagt tcggtatcta ctcttctaaa ccgtctgaag taaacatcgc tcagaacaac 240
gacatcatct acaacggtcg ttaccagaac ttctctatct ctttctgggt tcgtatcccg 300
aaatacttca acaaagttaa cctgaacaac gaatacacta tcatcgactg catccgtaac 360
aacaactetg gttggaaaat etetetgaac tacaacaaaa teatetggae tetgeaggae 420
actgctggta acaaccagaa actggttttc aactacactc agatgatctc tatctctgac 480
tacattaata aatggatctt cgttactatc actaacaacc gtctgggtaa ctctcgtatc 540
tacatcaacg gtaacctgat cgatgaaaaa tctatctcta acctgggtga catccacgtt 600
tctgacaaca tcctgttcaa aatcgttggt tgcaacgaca cgcgttacgt tggtatccgt 660
tacttcaaag ttttcgacac tgaactgggt aaaactgaaa tcgaaactct gtactctgac 720
gaaccggacc cgtctatcct gaaagacttc tggggtaact acctgctgta caacaaacgt 780
tactacctgc tgaacctgct ccggactgac aaatctatca ctcagaactc taacttcctq 840
aacatcaacc agcagcgtgg tgtttatcag aaacctaata tcttctctaa cactcgtctg 900
tacactggtg ttgaagttat catccgtaaa aacggttcta ctgacatctc taacactgac 960
aacttcgtac gtaaaaacga cctggcttac atcaacgttg ttgaccgfga cgttgaatac 1020
cgtctgtacg ctgacatctc tatcgctaaa ccggaaaaaa tcatcaaact gatccgtact 1080
tctaactcta acaactctct gggtcagatc atcgttatgg actcgatcgg taacaactgc 1140
actatgaact tccagaacaa caacggtggt aacatcggtc tgctgggttt ccactctaac 1200
aacctggttg cttcttcatg gtactacaac aacatccgta aaaacacttc ttctaacqqt 1260
tgcttctggt ctttcatctc taaagaacac ggttggcagg aaaactaaga attc
<210> 34
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<210> 34 <211> 432 <212> PRT <220>

<223> Encoded polypeptide of a synthetic construct based on BoNTF Hc

<400> 34 Met Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu 10 Tyr Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn 25 Asn Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn 40 Gly Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile 75 Tyr Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile 85 90 Pro Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile 105 Asp Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr 120 125 Asn Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys 135 140 Leu Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn 150 155 Lys Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg 165 170 Ile Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu 185 Gly Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys 200 Asn Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr 215 220 Glu Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp 230 235 Pro Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys 250 Arg Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln 265 Asn Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys . 280 Pro Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile 295 300 Ile Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val 310 315 Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu 325 330 Tyr Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile 345 Lys Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile 360 Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn 375 380 Asn Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val 390 395

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Ala Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn
                405
                                    410
Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn
                                425
<210> 35
<211> 1278
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTE Hc
<400> 35
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tccgttttaa acatgagata caagaatgat aaatacgtcg acacttccgg ttacgactcc 120
aatatcaaca ttaacggtga cgtgtacaag tacccaacta acaaaaacca attcggtatc 180
tacaacgaca agettactga getgaacate tetcaaaacq actacattat etacqacaac 240
aagtacaata acttetetat ttetttetgg gteagaatte etaactacga taacaagate 300
gtcaacgtta acaacgagta cactatcatc aactgtatga gagacaacaa ctccggttgg 360
aaggtetete ttaaccacaa cgagatgatt tggacettge aagacaacge aggtattaac 420
caaaagttag cattcaacta cggtaacgca aacggtattt ctgactacat caacaagtgg 480
attttcgtca ctatcactaa cgacagatta ggggactcta agctttacat taacggtaac 540
ttaatcgacc aaaagtccat tttaaactta ggtaacattc acgtttctga caacatctta 600
ttcaagatcg ttaactgcag ttacaacaga tacattggca ttagatactt caacattttc 660
gacaaggagt tagacgagac cgagattcaa actttataca gcaacgaacc taacaccaat 720
attttgaagg acttctgggg taactacttg ctttacgaca aggaatacta cttattaaac 780
gtgttaaagc caaacaactt cattgatagg agaaaggatt ctactttaag cattaacaac 840
atcagaagca ctattctttt agctaacaga ttatactctg gtatcaaggt taagatccaa 900
agagttaaca actettetae taacgataae ettgttagaa agaacgatea ggtetatatt 960
aacttcgtcg ctagcaagac tcacttattc ccattatatg ctgataacgc taccaccaac 1020
aaggagaaga ccatcaagat ctcctctct ggcaacagat ttaaccaagt cgtcgttatg 1080
aactccgtcg gtaacaactg taccatgaac tttaaaaata ataatggaaa taatattggg 1140
tgtttaggtt tcaaggcaga tactgtagtt gctagtactt ggtattatac ccacatgaga 1200
gatcacacca acagcaatgg atgtttttgg aactttattt ctgaagaaca tggatggcaa 1260
gaaaaataat agggatcc
                                                                  1278
<210> 36
<211> 419
<212> PRT
<213> Artificial Sequence
<220>
<223> Encoded polypeptide of a synthetic construct based
      on BoNTE Hc
Met Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys Ser
                                    10
Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp Thr
            20
                                25
Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys Tyr
Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Thr Glu
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Leu Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr Lys

70 75 Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn Lys 90 Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg Asp 105 Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile Trp 120 Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn Tyr 135 Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe Val 150 155 Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr Ile Asn Gly 165 170 Asn Leu Ile Asp Gln Lys Ser Ile Leu Asn Leu Gly Asn Ile His Val 185 Ser Asp Asn Ile Leu Phe Lys Ile Val Asn Cys Ser Tyr Thr Arg Tyr 200 Ile Gly Ile Arg Tyr Phe Asn Ile Phe Asp Lys Glu Leu Asp Glu Thr 215 Glu Ile Gln Thr Leu Tyr Ser Asn Glu Pro Asn Thr Asn Ile Leu Lys 230 235 Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu 245 250 Asn Val Leu Lys Pro Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr 260 265 Leu Ser Ile Asn Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu 280 Tyr Ser Gly Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr 295 Asn Asp Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val 310 315 Ala Ser Lys Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr 325 330 Asn Lys Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe Asn 340 345 Gln Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met Asn Phe 360 365 Lys Asn Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe Lys Ala Asp 375 Thr Val Val Ala Ser Thr Trp Tyr Tyr Thr His Met Arg Asp His Thr 390 395 Asn Ser Asn Gly Cys Phe Trp Asn Phe Ile Ser Glu Glu His Gly Trp Gln Glu Lys

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<210> 37
<211> 1338
<212> DNA
<213> Artificial Seque
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<213> Artificial Sequence

<220> <223> Synthetic construct based on BoNTA Hc

<400> 37
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cetecateet gaacetgege tacgaateea ateacetgat egacetgtet egetaegett 120
ccaaaatcaa catcggttct aaagttaact tcgatccgat cgacaagaat cagatccagc 180
tgttcaatct ggaatcttcc aaaatcgaag ttatcctgaa gaatgctatc gtatacaact 240
ctatgtacga aaacttctcc acctccttct ggatccgtat cccqaaatac ttcaactcca 300
tctctctgaa caatgaatac accatcatca actgcatgga aaacaattct ggttggaaag 360
tatctctgaa ctacggtgaa atcatctgga ctctgcagga cactcaggaa atcaaacagc 420
gtgttgtatt caaatactct cagatgatca acatctctga ctacatcaat cgctggatct 480
tegttaccat caccaacaat egtetgaata actecaaaat etacatcaac ggeegtetga 540
tegaceagaa acegatetee aatetgggta acatecaege ttetaataae ateatgttea 600
aactggacgg ttgtcgtgac actcaccgct acatctggat caaatacttc aatctgttcg 660
acaaagaact gaacgaaaaa gaaatcaaag acctgtacga caaccagtcc aattctggta 720
teetgaaaga ettetggggt gactacetge agtacgacaa accgtactae atgetgaate 780
tgtacgatcc gaacaaatac gttgacgtca acaatgtagg tatccgcggt tacatgtacc 840
tgaaaggtcc gcgtggttct gttatgacta ccaacatcta cctgaactct tccctgtacc 900
gtggtaccaa attcatcatc aagaaatacg cgtctggtaa caaggacaat atcgttcgca 960
acaatgatcg tgtatacatc aatgttgtag ttaagaacaa agaataccgt ctggctacca 1020
atgcttctca ggctggtgta gaaaagatct tgtctgctct ggaaatcccg gacgttggta 1080
atctgtctca ggtagttgta atgaaatcca agaacgacca gggtatcact aacaaatgca 1140
aaatgaatct gcaggacaac aatggtaacg atatcggttt catcggtttc caccagttca 1200
acaatatege taaactggtt getteeaact ggtacaateg teagategaa egtteetete 1260
gcactctggg ttgctcttgg gagttcatcc cggttgatga cggttggggt gaacgtccgc 1320
tgtaacccgg gaaagctt
<210> 38
<211> 415
<212> PRT
<213> Clostridium botulinum
<400> 38
Arg Tyr Glu Ser Asn His Leu Ile Asp Leu Ser Arg Tyr Ala Ser Lys
Ile Asn Ile Gly Ser Lys Val Asn Phe Asp Pro Ile Asp Lys Asn Gln
            20
                                25
Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile Glu Val Ile Leu Lys
                            40
Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn Phe Ser Thr Ser Phe
Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile Ser Leu Asn Asn Glu
                    70
                                        75
Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp Lys Val Ser
Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln Asp Thr Gln Glu Ile
            100
                                105
Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met Ile Asn Ile Ser Asp
                            120
                                                125
Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Asn
```

135

215

150

165

210

Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu Ile Asp Gln Lys Pro Ile

Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn Ile Met Phe Lys Leu

155

220

```
Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn Leu Tyr Asp Pro Asn Lys
                    230
                                         235
Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly Tyr Met Tyr Leu Lys
                                    250
Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile Tyr Leu Asn Ser Ser
            260
                                265
Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys Lys Tyr Ala Ser Gly Asn
                            280
Lys Asp Asn Ile Val Arg Asn Asp Arg Val Tyr Ile Asn Val Val
                        295
                                            300
Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn Ala Ser Gln Ala Gly
                    310
                                        315
Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro Asp Val Gly Asn Leu
                                    330
Ser Gln Val Val Met Lys Ser Lys Asn Asp Gln Gly Ile Thr Asn
Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly Asn Asp Ile Gly Phe
        355
                            360
                                                365
Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys Leu Val Ala Ser Asn
                        375
                                            380
Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser Arg Thr Leu Gly Cys Ser
                    390
                                        395
Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly Glu Arg Pro Leu
                                    410
                                                        415
<210> 39
<211> 1351
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTB Hc
<400> 39
atggetttea acaaatacaa tteegaaate etgaacaata teateetgaa eetgegttae 60
aaagacaaca atctgatcga tctgtctggt tacggtgcta aagttgaagt atacgacggt 120
gttgaactga atgacaagaa ccagttcaaa ctgacctctt ccgctaactc taagatccgt 180
gttactcaga atcagaacat catcttcaac tccgtattcc tggacttctc tgtttccttc 240
tggatccgta tcccgaaata caagaacgac ggtatccaga attacatcca caatgaatac 300
accatcatca actgcatgaa gaataactct ggttggaaga tctccatccg cggtaaccgt 360
atcatctgga ctctgatcga tatcaacggt aagaccaaat ctgtattctt cgaatacaac 420
atccgtgaag acatctctga atacatcaat cgctggttct tcgttaccat caccaataac 480
ctgaacaatg ctaaaatcta catcaacggt aaactggaat ctaataccga catcaaagac 540
atccgtgaag ttatcgctaa cggtgaaatc atcttcaaac tggacggtga catcgatcgt 600
acccagttca totggatgaa atacttotoo atottoaaca oogaactgto toagtocaat 660
atcgaagaac ggtacaagat ccagtcttac tccgaatacc tgaaagactt ctggggtaat 720
ccgctgatgt acaacaaga atactatatg ttcaatgctg gtaacaagaa ctcttacatc 780
aaactgaaga aagactctcc ggttggtgaa atcctgactc gttccaaata caaccagaac 840
tctaaataca tcaactaccg cgacctgtac atcggtgaaa agttcatcat ccgtcgcaaa 900
tctaactctc agtccatcaa tgatgacatc gtacgtaaag aagactacat ctacctggac 960
ttcttcaacc tgaatcagga atggcgtgta tacacctaca agtacttcaa gaaagaagaa 1020
gaaaagettt teetggetee gatetetgat teegaegaae tetacaacae catecagate 1080
aaagaatacg acgaacagcc gacctactct tgccagctgc tgttcaagaa agatgaagaa 1140
tctactgacg aaatcggtct gatcggtatc caccgtttct acgaatctgg tatcgtattc 1200
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gaagaataca aagactactt ctgcatctcc aaatggtacc tgaaggaagt taaacgcaaa 1260 ccgtacaacc tgaaactggg ttgcaattgg cagttcatcc cgaaagacga aggttggacc 1320

<210> 40

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<211> 439
<212> PRT
<213> Clostridium botulinum
<400> 40
Phe Asn Lys Tyr Asn Ser Glu Ile Leu Asn Asn Ile Ile Leu Asn Leu
Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala Lys
                                25
Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe Lys
Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln Asn
                        55
Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp Ile
                                        75
Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn
                                    90
Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys Ile
                                105
                                                    110
Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn Gly
                            120
                                                125
Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile Ser
                        135
                                            140
Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu Asn
                    150
                                        155
Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp Ile
                                    170
Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys Leu
                                185
Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe Ser
                            200
Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys
                        215
                                            220
Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu
                    230
                                        235
Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser
                245
                                    250
Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg
                                265
Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr
                            280
Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile
                        295
                                            300
Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe
                    310
                                        315
Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys Tyr Phe Lys Lys
                                    330
Glu Glu Glu Lys Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu Phe
                                345
Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr Ser
                            360
Cys Gln Leu Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile Gly
                        375
Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu Glu
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390 Tyr Lys Asp Tyr Phe Cys Ile Ser Lys Trp Tyr Leu Lys Glu Val Lys 405 410 Arg Lys Pro Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile Pro 420 425 Lys Asp Glu Gly Trp Thr Glu 435 <210> 41 <213> Clostridium botulinum

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Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser Glu Ile Leu Asn Asn Ile Ile Leu Asn Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe Ser Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys

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